Treatment Patterns Among Patients with Myelodysplastic Syndromes: Observations of 1st-Line Therapy, Discontinuation and the Need of Additional Therapies

Sudipto Mukherjee, MD, MPH[1]; Christopher R. Cogle, MD[2]; Tanya G.K. Bentley, PhD[3]; Michael S. Broder, MD, MSHS[3]; Eunice Chang, PhD[3]; Moira E. Lawrence, PhD[4]; Thomas J. McKearn, MD, PhD[4]; Scott Megaffin[4]; Rita Percy[4]; Michael E. Petrone, MD, MPH[4]; Gordon H. Sun, MD, MS[3]

[1] Cleveland Clinic Foundation, Cleveland, OH; [2]University of Florida, Gainesville, FL; [3] Partnership for Health Analytic Research, LLC, Beverly Hills, CA; [4] Onconova Therapeutics, Inc., Newtown, PA

BACKGROUND

- The myelodysplastic syndromes (MDS) typically affect older individuals.
- High-risk MDS patients are usually treated first with hypomethylating agents (HMAs; azacitidine [AZA] or decitabine [DEC]).[1]
- Presently, there are no approved therapeutic treatment options for those who have failed initial treatment with an HMA; 2nd-line therapeutic approaches are unproven and may include lenalidomide (LEN), switching to a different HMA, or supportive care.
- There is little published information on the treatment patterns of MDS patients after failed HMA therapy who become eligible for 2nd-line therapy.

OBJECTIVE

- To describe treatment patterns of MDS patients who have failed or become intolerant to HMA therapy.

METHODS

Study Design and Data Source

- Retrospective cohort study of a large US, HIPAA-compliant, commercial health insurance claims database.
- Timeframe: 1/1/2008 to ≥ 6 months after patients became candidates for 2nd-line MDS treatment, until the end of enrollment, or study end (12/31/2012).

Study Population

- We identified patients with an MDS-associated medical claim (ICD-9-CM diagnosis codes 238.7x) being treated with an HMA in the identification (ID) period (1/1/2009–12/31/2011) who were considered to have failed initial HMA treatment (AZA or DEC).
- The index date was the date on which patients were defined as eligible for 2nd-line therapy (i.e., initiated HMA treatment but then stopped for ≥ 2 months, switched to another HMA, or have been on the same HMA for > 7 months).

Outcomes

- 1st- and 2nd-line treatment patterns:
  - MDS-specific therapy: AZA, DEC, or LEN.
  - Utilization of hematologic supportive care agents, including erythropoiesis-stimulating agents (ESA), growth factors (i.e., granulocyte and granulocyte-macrophage colony-stimulating factors), and blood transfusions.
- 1st-line treatment only: Number of AZA or DEC cycles, defined as continuous treatment periods without a gap of >7 days, and the gap between observed cycles could not be ≥ 60 days.

RESULTS

Baseline Patient and Disease Characteristics

- Of 38,702 patients diagnosed with MDS in the ID period, 1,366 used an HMA (Figure 1).
- Among 402 patients eligible for 2nd-line MDS therapy (Figure 1), mean age was 72.9 years and 40% were female (Table 1).
- 386 (96.0%) patients had a cytopenia, including anemia (92.8%), neutropenia (53.0%), or thrombocytopenia (52.7%; Table 1).
- The mean Charlson comorbidity score was 3.6 (Table 1).
- AML/MDS dual diagnosis was present in 24.1% of patients at baseline (Table 1).

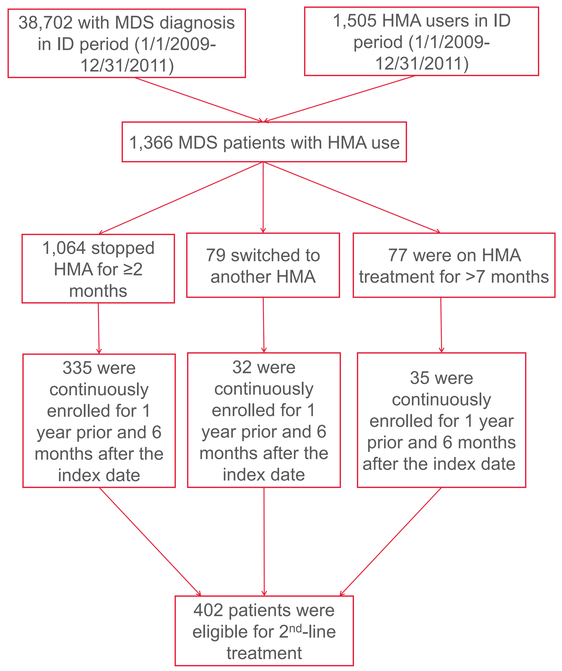
1st Line Treatment Patterns

- 283 (70.4%) and 123 (30.6%) of patients had used AZA and DEC, respectively.
- Patients averaged 6.1 (SD=5.1) HMA treatment cycles (6.4 (5.4) for AZA or 5.4 (4.0) for DEC) prior to being considered potential candidates for 2nd-line therapy.
- 193 (48.0%) patients had "early" discontinuation (47.1% for AZA, 50.0% for DEC), defined as less than (<) 5 treatment cycles before stopping or switching among HMAs.
- Among all 402 patients eligible for 2nd-line therapy, 320 (79.6%) received hematologic supportive care interventions: 208 (51.7%) received transfusions, 206 (51.2%) ESA, and 170 (42.3%) growth factors, at least one or more times.

Table 1. Patient and Disease Characteristics

Characteristic	Value
Age, year, mean (SD)	72.9 (9.1)
Female, no. (%)	160 (39.8)
Charlson comorbidity index, mean (SD)	3.6 (2.9)
Number of chronic conditions, mean (SD)	6.8 (2.3)
AML/MDS dual diagnosis, no. (%)	97 (24.1)
Cytopenias potentially associated with HMA use, no. (%)	386 (96.0)
Pancytopenia	202 (50.2)
Anemia	373 (92.8)
Thrombocytopenia	212 (52.7)
Leukopenia	93 (23.1)
Neutropenia	213 (53.0)

Figure 1. Patient Selection Flowchart



2nd Line Treatment Interventions

- Among 402 patients eligible for 2nd-line therapy, 32 (8.0%) switched to another HMA.
- The following treatments were received during 6 months' followup among these 402 patients:

  AZA: 121 (30.1%)

  DEC: 74 (18.4%)

  Lenalidomide: 18 (4.5%)

  Supportive care: 247 (61.4%; Table 2)

Table 2. Supportive Care Interventions

Characteristic	Value
Supportive Care, no. (%)	247 (61.4)
Blood Transfusions, no (%)	161 (40.0)
ESAs, no. (%)	122 (30.3)
Growth Factors, no. (%)	116 (28.9)

CONCLUSION

- These data suggest that a significant proportion of MDS patients are candidates for 2nd-line treatment after AZA and DEC.
- Discontinuation of 1st-line MDS treatment with less than (<) 5 HMA treatment cycles is frequent in higher-risk patients.
- AZA was used more often than DEC or LEN as 1st-line MDS therapy.
- The clinical reasons for early HMA discontinuation warrant further investigation, as does the frequency of need for co-administered hematologic supportive care interventions.
- Switching HMA occurs in a minority of patients after failing 1st line HMA therapy
- Safe and effective 2nd-line therapies that reduce cytopenias are needed for these patients.

REFERENCES

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